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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/755,855	01/12/2004	Stephen J. Lippard	MTV-061.01	8425

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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/755,855	LIPPARD ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *5-14,16,17,19-21,25-30,32,34 and 36-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4,15,18,22-24,31,33,35 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/18/05*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20051116* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

The restriction requirement mailed March 3, 2005 is herein withdrawn in favor of the instant requirement for the following reasons:

The requirement mailed on March 3, 2005 was returned to the USPTO as 'undeliverable'. In the interest of compact prosecution, and because the restriction was not received by Applicant, the Examiner contacted Applicant's Agent, Dr. M.J. Di Verdi, to obtain phone election, as outlined herein.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-35 and 42, drawn to platinum-based compounds and a kit, classified in class 424, subclass 629.

II. Claims 36-41, drawn to a method of treating cancer with compounds of Group I, classified in class 424, subclass 629.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)).

In the instant case one could treat cancer with a materially different compound, docetaxel.

The search for each of the above inventions is not co-extensive particularly with regard to the non-patented literature search. A reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

Additionally, the compounds of the instant application are distinct, absent evidence to the contrary, and would require a unique search strategy. The search for the distinct compounds is conducted based on their chemical structure. Therefore, the search of one chemical structure would not necessarily lead to the discovery of another structure, nor would it necessarily lead to the discovery of methods of using and/or making.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search for one invention would not necessarily lead to the discovery of another invention, restriction for examination purposes as indicated is proper, and to not restrict would be an undue burden on the Examiner.

Claims 1-42 are generic to a plurality of disclosed patentably distinct species comprising platinum compounds having cis-labile ligands, one or more therapeutic agents and/or targeting moieties and the presence or absence of a linker group. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Dr. M.J. Di Virdi, Applicant's Agent, on September 15, 2005, a provisional election was made with traverse to prosecute the invention of of Group I, with the species of BEP1, as found on page 63 of the specification. The species is readable upon **claims 1-5, 9-11, 15, 18, 22-24, 31, 33 and 35**. Affirmation of this election must be made by applicant in replying to this Office action. **Claims 6-8, 12-14, 16, 17, 19-21, 25-30,**

32, 34 and 36-41 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention or species. Please note, the elected species reads specifically on claims 9-11, which explicitly recite a linker lack clear antecedent basis (see 35 USC § 112, 2nd paragraph, rejection below). The examiner has interpreted for examination purposes only that claim 1 allows for the optional tether/linker between the Pt and therapeutic/targeting moiety.

Rejoinder Practice

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Sequence Compliance

Applicant is advised that the application is not in compliance with 37 CFR §§ 1.821-1.825.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR §§ 1.821- 1.825) in order to effect a complete response to this office action.

Specifically, sequences requiring SEQ ID NOs are found on, e.g. pages 4, 19, 59-61, 68 and 87, and in Table 1. Please note, Although the Examiner has thoroughly examined the specification for sequence compliance, the identified pages may not be fully inclusive.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (<http://www.uspto.gov/ebc/efs/downloads/documents.htm>, EFS Submission User Manual – ePave)

2. US Postal Service:
Commissioner for Patents
PO Box 22313-1450
Alexandria, VA 22313-1450

3. Hand carry, Federal Express, United Parcel Service, or other delivery service:
U.S. Patent and Trademark Office
Mail Stop Sequence
Customer Window, Randolph Building
401 Dulany Street
Alexandria, VA 22314

Specification

The disclosure is objected to because of the following informalities: The specification recites sequences without an accompanying SEQ ID NO, , e.g. pages 4, 19, 59-61, 68 and 87, and in Table 1.

Appropriate correction is required.

Claims 1-5, 9-11, 15, 18, 22-24, 31, 33 and 35 have been examined on the merits with regards to the elected species BEP1.

The examiner has determined that BEP1 is free of the prior art. The Examiner extended the search to include BEP2-BEP5 (Table 2, page 64), related to BEP1 via alkyl chain extension of the linker (*vida infra*, Examples 12-16). The Examiner found BEP2-5 to be free of the prior art. The Examiner extended the search to BEPn, as recited on page 23 of the instant specification, wherein the linker is any linker connected by an oxygen at the Pt center and the estradiol. BEPn has been found to be free of the prior art.

The examiner extended the search to the species cis[$Pt(NH_3)$(cyclaradine)$_2$]Cl_2 and the additional species ammine(2-amino-3-picoline)dichlorodiacetoplatinum(IV). The species are readable upon claims 1-4, 15, 18, 22-24, 31, 33, 35 and 42.

Claims 5 and 9-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Claims 1-4, 15, 18, 22-24, 31, 33, 35 and 42 have been examined on the merits with regards to the species cis[$Pt(NH_3)$(cyclaradine)$_2$]Cl_2 and ammine(2-amino-3-picoline)dichlorodiacetoplatinum(IV).

Please note, claims 5-14, 16, 17, 19-21, 25-30, 32 and 34 have been examined insofar as formal matters and rejections under 35 USC § 112, for Applicant's benefit. This inclusion does not imply that the claims have been examined with respect to the prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-14, 35 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 12 recite 'covalently attached through a tether', which lacks clear antecedent basis. Claim 1, from which they both depend, recites that the therapeutic/targeting moiety is covalently attached to the Pt, and does not allow for the tether to be interposed in the structure.

Claims 25-30 recite 'tethered steroid' or 'tethered peptide'. There is insufficient antecedent basis for this limitation in the claims. Claim 15, from which they depend recites that R and M are a therapeutic agent, a targeting moiety, or a labile covalently bonded ligand. Claim 15 does not allow for the redefining of R and M with new definitions.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 15, 18, 22-24, 31, 33, 35 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by TALROY (US Patent 4,873,226).

The instant claims are drawn generally to cisplatin analogs with a Pt(IV) hexacoordinate metal center, with two therapeutic moieties attached to the metal.

Talroy teaches cis[$Pt(NH_3)(cyclaradine)_2$]Cl_2 in a purified form(column 6, line 16) and in a pharmaceutical composition (e.g. claim 5). The compound is used in the method of inhibiting herpetic lesions (claims 4 and 5). Cyclaradine is an antiviral. Talroy teaches that other antivirals (listed in column 2, lines 33-42) can be used in the invention in place of cyclaradine.

Because the structure of Talroy meets all of the instantly claimed limitations, it must inherently release the cyclaradine upon reduction of Pt(IV) to Pt(II). Further, because the 'kit' requires only the Pt compound, and instructions, a teaching of the compound meets the limitations, as the MPEP states,

"Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. *In re Ngai*, ___ F.3d ___, 2004 WL 1068957 (Fed. Cir. May 13, 2004)(Claim at issue was a kit requiring instructions and a buffer agent. The Federal Circuit held that the claim was anticipated by a prior art reference that taught a kit that included instructions and a buffer agent, even though the content of the instructions differed.). See also *In re Gulack*, 703 F.2d 1381, 1385-86, 217 USPQ 401, 404 (Fed. Cir. 1983)("Where the printed matter is not functionally related to the substrate, the printed matter will not distinguish

the invention from the prior art in terms of patentability .... [T]he critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate.")." (MPEP § 2112.01).

Claims 1-4, 15, 18, 22-24, 31, 33, 35 and 42 are rejected under 35 U.S.C. 102(e) as being anticipated by LIPPARD (US Patent 6,806,289 B1) in view of DOSCH (US Patent 6,469,066 B1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claims are presented *supra*.

Lippard teaches the compound ammine(2-amino-3-picoline)dichlorodiacetoplatinum(IV) in a pharmaceutical composition (claim 12).

Dosch is relied upon for the beneficial teachings that acetic acid (aceto group, of Lippard) is a therapeutic for treating burns (Abstract, Dorsch).

The Pt is Pt(IV), having 2 axial ligands comprising carboxylates (claim 9) and in a pharmaceutical composition (claim 12).

Because the structure of Lippard meets all of the instantly claimed limitations, it must inherently release the acetate (acetic acid) upon reduction of Pt(IV) to Pt(II). Further, because the 'kit' requires only the Pt compound, and instructions, a teaching of the compound meets the limitations, as the MPEP states, .

"Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. *In re Ngai*, ___ F.3d ___, 2004 WL 1068957 (Fed. Cir. May 13, 2004)(Claim at issue was a kit requiring instructions and a buffer agent. The Federal Circuit held that the claim was anticipated by a prior art reference that taught a kit that

included instructions and a buffer agent, even though the content of the instructions differed.). See also *In re Gulack*, 703 F.2d 1381, 1385-86, 217 USPQ 401, 404 (Fed. Cir. 1983)("Where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability .... [T]he critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate.")." (MPEP § 2112.01).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 15, 18, 22-24, 31, 33, 35 and 42 are rejected on the ground of nonstatutory double patenting over claims 1 and 9-12 of U. S. Patent No. 6,806,289 B1 (LIPPARD, *supra*) in view of DORSCH, *supra*, since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows:

The instant claims and teachings of Lippard and Dorsch are set forth *supra* (*see* 35 USC § 102(e)). The compound in the pharmaceutical of Lippard (claim 12) is a species of the instantly claimed Pt hexacoordinate complexes, and thus anticipates the instant claims for the reasons set forth *supra* under 35 USC § 102(e).

Allowable Subject Matter

As indicated *supra*, BEP1-BEP5 and BEPn, where the compound general structure is estradiol-O-(anything)-O-Pt (structure of Scheme 1, page 23), are free of the prior art.

The following is a statement of reasons for the indication of allowable subject matter:

The closest prior art of record, LIPPARD (US Patent 6,806,289 B1) and TALROY (US Patent 4,873,226) do not teach or suggest, alone or in combination, the instantly claimed structures of estradiols linked to Pt centers in a Pt(IV) cisplatin complex through a linker moiety.

Conclusion

The prior art made of record on the attached PTO-892 and not relied upon in any rejection is considered pertinent to applicant's disclosure.

Specifically: KWON (US Patent 6,340,770 B1 teaches cisplatin(IV)(trifluoroacetate)$_2$ and other trifluoralkyl acid coplexes (e.g. claim 2 at line 30); BERMAN (US Patent 6,384,081 B2) teaches that TFA is a therapeutic (e.g. column 12 at line 23).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ADK
Andrew D. Kosar, Ph.D.
Art Unit 1654

Bruce Campell

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